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EXAMINER	
TON, THAIAN N	
ART UNIT	PAPER NUMBER
1632	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/675,509	FULTON ET AL.	
	Examiner	Art Unit	
	Thaian N. Ton	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 May 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *10 and 33-40* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *10,33 and 36-39* is/are allowed.

6)☒ Claim(s) *34,35 and 40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants' Remarks filed 5/21/09 have been entered. No claims have been amended. Claims 10, 33-40 are pending; claims 10, 33 and 36-39 are allowed; claims 34, 35 and 40 are under current examination.

Written Description

Claims 34 and 40 stand rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicants Arguments. Applicants argue that the proper standard for determining compliance with the written description requirement is whether the specification reasonably conveys to the skilled artisan that the inventor was in possession of the claimed invention as of the filing date and that the subject matter need not be described literally in the specification in order to fulfill this requirement. See p. 4 of the Response.

Applicants argue that instant claim 34 is directed to a purified, enriched or isolated nucleic acid sequence, wherein each and every nucleotide of SEQ ID NO: 3 is known and unambiguously described in the Application and that selecting a portion of SEQ ID NO: 3 that is 200 nucleotides in length is a trivial task to one of ordinary skill in the art as is determining the number of nucleotide bases that would constitute 90% of the selected portion of SEQ ID NO: 3, accordingly Applicants argue that the specification provides sufficient written description for the claimed invention. See p. 5, 1st paragraph of the Response.

Applicants argue that one of ordinary skill in the art could readily make a protein at least 200 nucleotides in length having 90% or 95% sequence identity to SEQ ID NO: 3, and test for thiaminase activity, such as depicted in Examples 1-3 of

the spec, and as such, the ordinary skilled artisan could readily determine whether a particular protein encoded by a nucleic acid sequence does not have the requisite thaiminase activity without undue experimentation. See p. 5, ¶2 of the Response.

Applicants argue that the Examiner's assertion that a 200 nucleotide segment is 18.7% of the total length is irrelevant to the determination as to whether there is adequate written description for the claimed invention because each and every nucleotide of SEQ ID NO: 3 is provided in the Application, therefore, every possible 200 nucleotide segment of SEQ IDNO: 3 is also inherently described. See p. 5-6 of the Response.

Response to Arguments. These arguments have been considered, but are not persuasive. In particular, claim 34 is included in the instant rejection in view of the implied functional limitation presented in claim 40, namely that the sequence encodes a protein having thiaminase activity. The specification discloses the reduction to practice of one species within the claimed genus; specifically the protein encoded by the full length SEQ ID NO:3.

The claims are drawn to a genus of polynucleotides that is defined only by sequence identity. However, the instant specification fails to describe the entire genus of proteins (*i.e.*, fragments, derivatives of variants of the polynucleotide) which are encompassed by the claims. Thus, the genus of these polynucleotides which, when constructed and used as claimed, lacks a written description, and as such, there is no indication that Applicants had possession of the claimed invention.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claims is a reference to structure in the form of a recitation of partial structural

similarity, "fragment", or vague structural resemblance, "derivative or variant". There is not even identification of any particular portion of the structure that must be conserved. Given that there is no art-recognized correlation between any structure (other than the full length SEQ ID NO: 3) and the thiaminase activity, based upon which those of ordinary skill in the art could predict which nucleic acids can vary from SEQ ID NO: 3 without losing thiaminase activity. Consequently, there is no information about which nucleic acids can vary from SEQ ID NO: 3 in the claimed genus of nucleic acids and still retain thiaminase activity.

The skilled artisan cannot envision the detailed chemical structure of all of the fragments, derivatives or variants, that are encompassed by the claims, and therefore, conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method. Adequate written description requires more than a mere statement that it is part of the invention, and a reference to a potential method of isolating it. See *Fiers v. Revel,* 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016 (Fed. Cir. 1991).

The recitation of a purified, enriched or isolated nucleic acid sequence that is at least 90% identical to a portion at least 200 nucleotides in length of the *N. gruberi* thiaminase sequence as set forth in SEQ ID NO: 3, and more specifically, wherein the protein has thiaminase activity, at the most, represents a partial structure. That is, the Examiner's previous analysis applies as follows:

1. SEQ ID NO: 3 is 1068 nucleotides in length.
2. 200 nucleotides of the total length is approximately 18.7%
3. 90% identical to an equal length of 200 nucleotides is 180 nucleotides.

Thus, Applicants are claiming a sequence that is at least 180 nucleotides identical to an equal length sequence that is only, minimally, 18.7% of the total length of SEQ ID NO: 3. There is no teaching in the specification regarding which portion(s) of the resultant peptide can vary. There is no teaching in the

specification with regard to what portion (at minimum, 18.7% of SEQ ID NO: 3 and 200 nucleotides in length) can be varied, while retaining the property of thiaminase activity. Furthermore, there is no art-recognized correlation between any structure (other than the full length SEQ ID NO: 3) and the thiaminase activity, based upon which those of ordinary skill in the art could predict which nucleic acids can vary from SEQ ID NO: 3 without losing thiaminase activity. Consequently, there is no information about which nucleic acids can vary from SEQ ID NO: 3 in the claimed genus of nucleic acids and still retain thiaminase activity.

Although the disclosure of a single disclosed species may provide an adequate written description for the genus, this is only the case when the species disclosed is representative of the genus. In the instant case, the genus encompasses sequences that have 90% homology to 200 nucleotides of SEQ ID NO: 3. These nucleic acids may encompass for example, polymorphisms and allelic variants. The specification does not provide any guidance for any of the fragments that are encompassed by the claims, other than the full length SEQ ID NO: 3. For example, there is no description of various mutational sites in an allele that would occur in nature, and the general knowledge in the art concerning alleles does not provide any indication of how the structure is representative of unknown alleles. The nature of alleles is that they are variant structures, and in the present state of the art, the structure of one does not provide structure to the others. The common attributes of the genus claimed are not described, and therefore one of skill would conclude that Applicants were not in possession of the claimed genus because the only description that exists is that of the full length, 100% identical SEQ ID NO:3.

Although the disclosure of SEQ ID NO: 3 combined with the knowledge in the art would put one in possession of nucleic acid sequences that is at least 90% identical to a portion at least 200 nucleotides in length of SEQ ID NO: 3, the level and skill and knowledge in the art is such that one of ordinary skill would not be able to identify without further testing, which of the proteins encoded by the nucleic

acid sequences (if any) would have thiaminase activity. Based upon the lack of knowledge and predictability in the art, those of ordinary skill in the art would not conclude that Applicants were in possession of the claimed genus of nucleic acid sequences claimed, based upon the disclosure of the single species of the full length SEQ ID NO: 3.

Accordingly, it is maintained that the claims fail to be described by the as-filed disclosure.

Enablement

Claims 34, 35 and 40 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an purified, enriched or isolated nucleic acid sequence consisting of SEQ ID NO: 3, does not reasonably provide enablement for fragments of SEQ ID NO: 3, wherein the nucleic acid sequence is at least 90% identical to a portion at least 200 nucleotides in length of the *N. gruberi* thiaminase sequence (SEQ ID NO: 3). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Enablement is considered in view of the Wands factors (MPEP 2164.01(A)). These include: nature of the invention, breadth of the claims, guidance of the specification, the existence of working examples, state of the art, predictability of the art and the amount of experimentation necessary. All of the Wands factors have been considered with regard to the instant claims, with the most relevant factors discussed below.

Applicants' Arguments. Applicants argue that the claims are limited to very specific nucleic acid sequences that have a high level of homology (*i.e.*, 90%) to a single specific nucleic acid sequence, and that the scope of the claims is clear and finite, and that the claims are enabled (p. 6 of the Response).

Applicants argue that the specification provides working examples of assays for detecting and measuring thiaminase activity and cite several other methods available for assaying thiaminase activity. Applicants argue that the specification also provides a working example for making and expressing recombinant nucleic acid sequences encompassed by the claims, and an example of a Cys to Ser mutation that inactivates enzymatic activity, thus providing a site possibly responsible for enzymatic activity. See pages 7-8 of the Response.

Response to Arguments. These arguments have been fully considered but are not fully persuasive. In particular, the specification only provides guidance for substituting amino acids within the same sequence. The specification does not provide guidance for the various fragments or variants encompassed by the claims that is at least 90% identical to 200 nucleotides of SEQ ID NO: 3. In particular, the state of the art is such that only two thiaminases have ever been described in the art, and that the particular thiaminase with which the instant Application is concerned has no high degree of homology to any other known thiaminase. Although the specification provides guidance for utilizing nucleic acid sequences that encode polypeptides that have thiamin-binding activity for various *in vitro* and *in vivo* uses, the breadth of the instant claims encompasses any nucleic acid sequence fragment, which may, or may not, have thiaminase activity. The specification does not provide guidance as to how to use nucleic acid sequence fragments, or proteins encoded therein, which may not have thiaminase activity.

With regard to Applicants arguments which state that one of ordinary skill in the art could readily identify, make and use fragments and variants encompassed by the claims by virtue that one could systematically identify each and every possible fragment and variant of SEQ ID NO: 3 encompassed by the claims, the Examiner notes that the claims broadly encompass nucleic acid fragments that may or may not encode a thiaminase. That is, the function of the protein encoded by the nucleic acid is found in dependent claims, and therefore the broadest claims

encompass nucleic acid fragments that do not have thiaminase activity. The specification does not provide any guidance for nucleic acid fragments that do not encode a thiaminase, or encode a peptide that does not have thiaminase activity. Given that the specification provides no guidance for specific functional domains of thiaminase I from *N. gruberi*, and that the instantly claimed thiaminase I has no significant homology to any known peptide; and only ~25% homology to a portion of the *Bacillus* thiaminase I, one of skill in the art would have had to practice undue experimentation to determine which of the variants or fragments encompassed by the claims, would encode a thiaminase I, or derivative thereof, which would have thiaminase I activity. One of skill in the art could not rely upon the state of the art because the state of the art does not provide specific guidance for thiaminases, in general, and specifically, with regard to thiaminase I.

Additionally, one of skill in the art would have had to practice undue experimentation to determine how to use nucleic acid fragments that did not have encode proteins with thiaminase activity, because the specification only contemplates fragments that encode functional proteins. Given that the specification only provides guidance for the full length SEQ ID NO: 3 and its encoded protein, it would have required undue experimentation for one of skill in the art to determine which, if any, of the fragments encompassed by the claims would have thiaminase activity, such that these fragments could be used in any of the methods contemplated by the specification.

Accordingly, in view of the view of the lack of specific guidance or teaching provided by the specification with regard to specific domains and structure of thiaminases in general, and specifically, with regard to thiaminase I, the lack of correlation between any fragments encompassed by the claims and an enabled use for these fragments, and the art of thiaminases, which clearly show that thiaminase I from *N. gruberi* does not have significant homology to any known thiaminase, it

would have required undue experimentation for one of skill in the art make and use the claimed invention.

Conclusion

Claims 10, 33, 36-39 are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Thaian N. Ton whose telephone number is (571)272-0736. The examiner can normally be reached on 9-5:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on 571-272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Thaian N. Ton/
Primary Examiner, Art Unit 1632